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Characteristics of frequency-of-seeing curves for a motion stimulus in glaucoma eyes, glaucoma suspect eyes, and normal eyes

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Abstract

This study compared frequency-of-seeing curves for a line displacement test in glaucoma patients and normals. Probit analysis of the frequency-of-seeing curves provided the motion thresholds and the slopes of the frequency-of-seeing curves, represented by the interquartile range. The thresholds and interquartile ranges were significantly elevated in the glaucoma eyes and suspect eyes, compared to controls. A logistic regression model incorporating both the interquartile range and threshold significantly improved the sensitivity of the motion test in the suspects. Abnormal shallowing of the slope of the motion frequency-of-seeing curve may represent one of the earliest changes in glaucoma. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Histological evidence has shown that a substantial number of retinal ganglion cell axons may be lost in glaucoma before a visual field defect can be detected using conventional methods of full threshold automated perimetry (Quigley, Addicks & Green, 1982; Quigley, Dunkelberger & Green, 1989). This finding has prompted the development of alternative tests, including motion detection, which may be more sensitive in detecting early glaucomatous visual damage. We have previously demonstrated glaucomatous loss of motion sensitivity using a line displacement test (Fitzke, Poinoosawmy, Ernst & Hitchings, 1987; Fitzke, Poinoosawmy, Nagasubramanian & Hitchings, 1989; Ruben & Fitzke, 1994; Baez, McNaught, Dowler, Poinoosawmy, Fitzke & Hitchings, 1995), and a number of workers have confirmed these findings using line stimuli (Johnson, 1994; Johnson, Marshall & Eng, 1995) and random dot kinetograms (Silverman, Trick & Hart, 1990; Bullimore, Wood & Swenson, 1993; Trick, Steinman & Amyot, 1995; Wall & Ketoff, 1995; Bosworth, Sample & Weinreb, 1997; Joffe, Raymond & Chrichton, 1997).

Experimental work in primates has shown that magnocellular ganglion cells are primarily responsible for the perception of motion elicited by small line displacements (Lee, 1993; Lee, Wehrhahn, Westheimer & Kremers, 1993). This is consistent with evidence from other studies which suggests that primate perception of motion to a variety of stimuli is primarily a function of the magnocellular system (Livingstone & Hubel, 1987; Merigan & Maunsell, 1990; Merigan, Byrne & Maunsell, 1991). However motion sensitivity may not be exclusively a property of the magnocellular system, as parvocellular mechanisms have also been shown to participate in such functions (Lee, Wehrhahn, Westheimer & Kremers, 1993; Anderson, Drasdo & Thompson, 1995).

A principal hypothesis to account for the early occurrence of motion sensitivity defects is the concept of preferential loss of larger diameter magnocellular ganglion cells, in early glaucoma, which has received support from a number of histological studies (Quigley, Dunkelberger & Green, 1988, 1989; Glovinsky, Quigley & Dunkelberger 1991; Chaturvedi, Hedley & Dreyer, 1993; Glovinsky, Quigley & Pease, 1993). An alternative hypothesis to account for a variety of early deficits of visual function in glaucoma is based on the concept of reduced redundancy (Johnson, 1994).

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The redeuced redundancy theory postulates that those tests which isolate a very sparse population of ganglion cells, with little physiological redundancy, will identify the earliest loss in glaucoma. Such selective tests have identified deficits of motion sensitivity (a test of magnocellular ganglion cell function) (Fitzke, Poinoosawmy, Ernst & Hitchings, 1987; Fitzke, Poinoosawmy, Nagasubramanian & Hitchings, 1989; Silverman, Trick & Hart, 1990; Bullimore, Wood & Swenson, 1993; Ruben & Fitzke, 1994; Johnson, 1994; Johnson, Marshall & Eng, 1995; Trick, Steinman, & Amyot, 1995; Wall & Ketoff, 1995; Bosworth, Sample & Weinreb, 1997; Joffe, Raymond & Chrichton, 1997), blue-on-yellow sensitivity (a test of the short wavelength sensitive ganglion cells) (Sample & Weinreb, 1992; Johnson, Adams, Casson & Brandt, 1993b,a), and flicker sensitivity (Lachenmayr, Drance, Douglas & Mikelberg, 1991; Casson, Johnson & Shapiro, 1993; Tyler, Hardage & Stamper, 1994).

Previously published investigations of motion sensitivity losses in glaucoma have concentrated on differences in the motion thresholds between groups. Although Silverman, Trick & Hart (1990) reported a qualitative lessening of the slope of the psychometric curve of motion in some patients with glaucoma, there has been no detailed analysis of frequency-of-seeing curves for a motion response in glaucoma to date. Frequency-of-seeing curves describe the relationship between the probability of seeing a stimulus and a stimulus parameter such as intensity (luminance stimulus) or stimulus displacement (motion stimulus). The S-shaped frequency-of-seeing curve has been shown to describe the relationship between luminance sensitivity and variability in automated perimetry (Chauhan & House, 1991; Weber & Rau, 1992; Olsson, Heijl, Bengtsson & Rootzen, 1993; Chauhan, Tompkins, LeBlanc & McCormick, 1993; Henson, Evans, Chauhan & Lane, 1996; Wall, Maw, Stanek & Chauhan, 1996). The threshold is usually defined as the stimulus intensity at which 50% of the stimuli will be seen. In addition the steepness of the frequency-of-seeing curve can be calculated to provide a measure of the intratest variability around the threshold at that test location. A steep gradient represents little variability, whilst shallow gradients indicate large intratest variability. A number of workers have found a significant correlation between threshold and the slope of the frequency-of-seeing curve for luminance stimuli (Chauhan & House, 1991; Weber & Rau, 1992; Olsson, Heijl, Bengtsson & Rootzen, 1993; Chauhan, Tompkins, LeBlanc & McCormick, 1993; Henson, Evans, Chauhan & Lane, 1996; Wall, Maw, Stanek & Chauhan, 1996). These studies have reported a shallowing of the slope of the frequency-of-seeing curve in glaucoma patients with decreased sensitivities, reflecting an abnormally high intratest variability. In addition, Chauhan, Tompkins, LeBlanc & McCormick (1993) have shown that glaucoma patients have widely differing frequency-of-seeing curves for similar thresholds and were able to identify patients who had normal Humphrey field thresholds, but who had an abnormally shallow slope of the frequency-of-seeing curve . This study tests the hypothesis that frequency-of-seeing analysis can characterise additional differences between the motion response of normal subjects and glaucoma patients, beyond that achieved by measuring thresholds alone. The identification of these differences may allow us to improve the sensitivity and specificity of motion testing in glaucoma.

2. Methods

2.1. Testing strategy

We measured motion sensitivity using a line displacement test presented in the superotemporal field to obtain Motion Displacement Thresholds (MDT). This site was chosen as previous results have identified significantly elevated Motion Displacement Thresholds at this location in glaucoma patients, with good separation between patients and controls (Fitzke, Poinoosawmy, Ernst & Hitchings, 1987; Fitzke, Poinoosawmy, Nagasubramanian & Hitchings, 1989). The MDT test was performed using a computer generated line stimulus presented on a monochrome monitor (Phillips green monochrome P31 monitor, model number 750205, pixelation 300×920, frame rate 50 Hz). The view distance was 1.24 m. The width of the stimulus was formed by addressing two horizontal pixels. The stimulus subtended $2^\circ \times 2$ min arc in size and the background $8 \times 10^\circ$, as measured directly from the display. The line stimulus was presented in the superotemporal field at 15° eccentricity on the 30° meridian. The luminance of the background was 7 cd/m^2 and the stimulus was 27 cd/m^2.

The subject viewed a fixation target and was instructed to press a response button when movement was seen. A warning tone was sounded which was followed by 1.5 s during which the stimulus was stationary. During the following 2 s, the stimulus (if it were to move), would undergo sudden oscillatory displacements at 2.5 Hz. beginning at a random time after the start of this interval. If the subject pressed the response button before stimulus movement had begun, then this was counted as a false positive response.

After a suitable instruction period, subjects underwent a test which consisted of ten presentations each of ten different displacements in 2 min arc intervals from 0 to 18 min arc presented in a random order. The test includes ten presentations of a 0 min arc displacement (stationary target catch trials) and if the subject presses the button to 0 min arc displacement then this was

recorded as a false positive response. The experimenter observed the subject for the duration of the test to ensure reliable fixation throughout the test.

2.2. Subjects

The study was approved by the Moorfields Hospital Ethics Committee and followed the tenets of the Declaration of Helsinki. All patients and controls gave informed consent prior to agreeing to participate. We defined a glaucoma eye as primary open-angle glaucoma (POAG) if it fulfilled the following diagnostic criteria:

1. Documented evidence of an intra-ocular pressure >21 mmHg on at least one occasion in the presence of an open angle.
2. Abnormal optic disc with glaucomatous optic disc cupping.
3. Previously documented glaucomatous visual field defect on the Humphrey 24-2 field test.

A field was defined as glaucomatous on the Humphrey 24-2 if at least one hemifield contained a cluster of a minimum of three adjacent depressed points on the STATPAC2 pattern deviation plot with one point having a probability of $P<1\%$ and two adjacent points having a probability of $P<2\%$ (Piltz, Drance, Douglas & Milkelbergh, 1991). We evaluated the Humphrey 24-2 field at the MDT test site using the field thresholds of the four locations nearest the MDT test site (see Fig. 1A). We defined the Humphrey 24-2 field at the motion test site as being abnormal if the field thresholds of at least one of these four locations was contiguous with a hemifield cluster of depressed locations, according to the above criteria.

Glaucoma suspect eyes were eligible if they had at least one of the following: glaucomatous optic disc cupping, clinical evidence of retinal nerve fiber layer defects, or a documented intra-ocular pressure >21 mmHg on at least one occasion, in the presence of a normal Humphrey 24-2 field (defined as normal or borderline Glaucoma Hemifield Test in the absence of any clusters of depressed locations in either hemifield). We excluded any eyes with significant ocular pathology other than glaucoma, including evidence of cataract or secondary glaucoma, and eyes which were being treated with topical miotics. We recruited suitably age matched controls if they had no significant ocular history, had a normal ocular examination with an IOP less than 21 mmHg and had normal Humphrey HFA 24-2 fields (defined as a normal Glaucoma Hemifield Test with

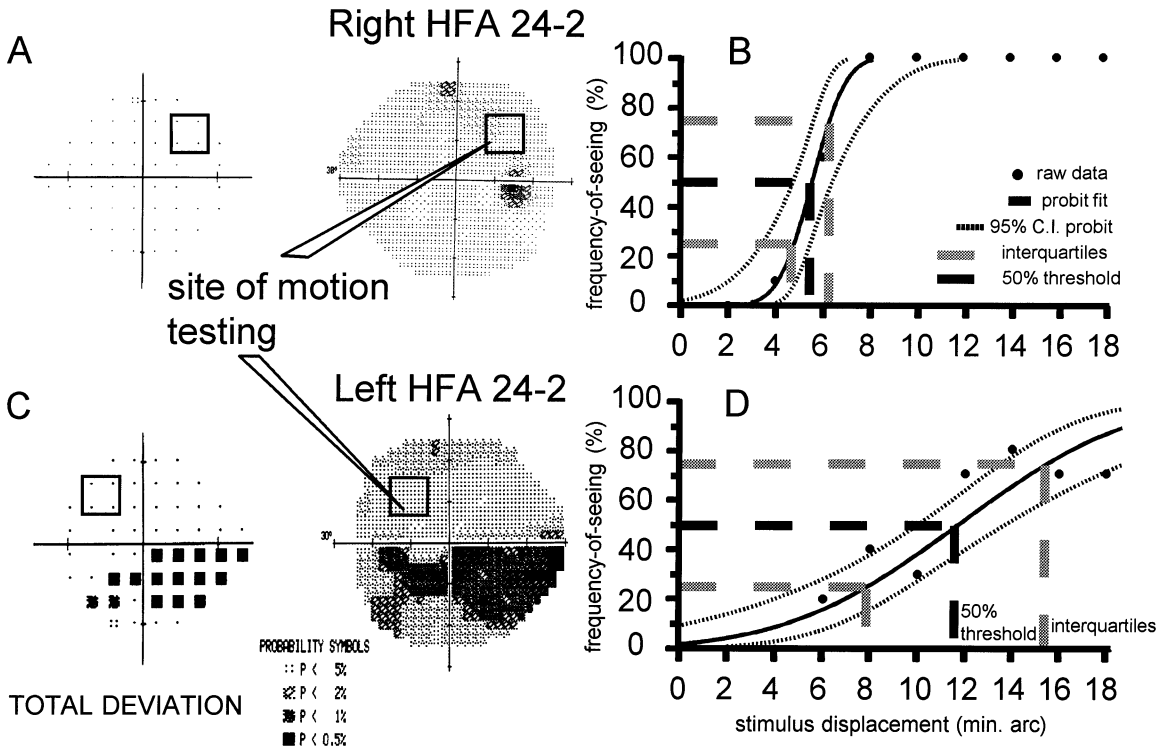

Fig. 1. (A) Humphrey 24-2 greyscale and Statpac2 total deviation plot from normal control aged 69, showing site of motion testing (arrow) with four closest Humphrey test locations; (B) normal subject's motion frequency-of-seeing curve. Black circles represent raw data points with probit-fitted curve (solid black curve), and 95% CI (dashed black curves). Dashed black line indicates normal 50% seen threshold of $5.5\pm$SE 0.4 min arc with normal interquartile range of $1.5\pm$SE 0.5 min arc (dashed grey lines); (C) humphrey 24-2 of a glaucoma patient aged 69 with an inferior arcuate scotoma. Arrow indicates site of motion testing on greyscale plot, with four closest Humphrey 24-2 test locations (box) showing normal threshold sensitivity, within 95% population limits on Statpac2 output; and (D) motion frequency-of-seeing curve of same patient, with elevated threshold ($11.6\pm$SE 0.9 min arc) and abnormally shallow slope, indicated by elevated interquartile range of $7.6\pm$SE 1.3 min arc.

global indices within 95% CI for normal subjects with no hemifield clusters of depressed points). All Humphrey 24-2 fields met standard reliability criteria of $<20\%$ fixation losses, $<33\%$ false negatives, $<33\%$ false positives. All patients and controls had a corrected visual acuity in the tested eye of $\geq 6/9$ achieved with less than ± 4 dioptres spherical equivalent and less than 2 dioptres of astigmatism. We tested 29 control subjects and 42 patients. The controls underwent testing in one randomly selected eye. Twenty-seven patients had one eye meeting either POAG ($n=14$) or glaucoma suspect criteria ($n=13$) and underwent testing in this eye only. Fifteen patients had POAG in one eye and a glaucoma suspect fellow eye, and underwent testing of both eyes in a randomised order. Because these patients were contributing both eyes to the study, we performed two independent analyses of the data: the first using data from both eyes of these patients, then reanalysing using data from only one eye selected at random from each of these patients. We present the data using both eyes of these patients, as all statistically significant results reported in this study were confirmed using both analyses, and did not differ at the $P=0.005$ level of significance.

The mean age of the controls was 58.7 ± 10.5 years, with a range 31.3–74.9 years. The mean age of patients with glaucoma suspect eyes tested was 60.9 ± 11.5 years (range 30.6–78.8 years) and POAG eyes tested was 62.9 ± 10.7 years (range 30.6–78.8). Analysis of variance showed no statistically significant differences between the group's ages at the 0.05 level. The Humphrey 24-2 Mean Defects (MD or weighted average deviation from the age-corrected normal reference field) of the glaucoma eyes ranged from -14.2 to -1.3 dB, (median -4.6 dB), and the glaucoma suspect eyes from -4.2 to $+1.8$ dB (median -0.7 dB). The MDs of the glaucoma eyes and suspect eyes were significantly lower than the Humphrey 24-2 MDs of the control eyes (range $-2.7-+2.5$ dB, median 0.05 dB) at the $P<0.05$ level. Although all suspects had Humphrey 24-2 fields that fulfilled our definition of normality, five (of 28) had a depressed MD, one had a depressed PSD, and five had a depressed CPSD at the $P<0.05\%$ level.

2.3. Analysis

We generated frequency-of-seeing curves of the subject's responses to the motion stimulus, and the data were imported to SPSS for Windows, (release 6.0, SPSS, Chicago, IL) for further analysis. We performed probit analysis of the data using SPSS and the motion displacement threshold (MDT) was defined as the displacement corresponding to a 50% frequency-of-seeing of the probit fitted curve. We used the interquartile range as a measure of the slope of the frequency-of-seeing curve, as this measure has previously been used by other investigators (Chauhan, Tompkins, LeBlanc & McCormick, 1993). The interquartile range is the stimulus displacement interval that corresponds to 25–75% frequency-of-seeing of the probit fitted curve. Fig. 1B shows the motion frequency-of-seeing curve from a normal control, with the calculated parameters. Fig. 1A shows the site of motion testing, superposed to the subject's Humphrey 24-2 plot. Because the variances of the groups were dissimilar for both the motion thresholds and interquartile ranges (Levene Test for Homogeneity of Variances $P<0.05$), non parametric Kruskal–Wallis tests were performed to identify for significant differences between the three groups. Post-hoc Mann–Whitney U tests were then performed to identify the significant differences between pairs of groups.

To characterise the extent to which the slope provides additional information we analysed the data according to a stepwise logistic regression model incorporating both the motion thresholds and the interquartile ranges, and their squared terms. This was performed for normal against glaucoma eyes, and for normal against suspect eyes. The results of the logistic regression analysis were used to generate a receiver operating characteristic (ROC) curve which was compared to the ROC curve generated using the motion threshold alone. The ROC curve is a plot of sensitivity versus one-specificity for each possible cut-off across the measurement range of the variables, and is useful in comparison of two or more test parameters (Graham, Drance, Chauhan, Swindale, Hnik, Mikelberg & Douglas 1996). The overall ability of a parameter to separate normals from patients was summarised by calculating the area under the ROC curve. According to this analysis, the discriminating ability of a parameter is represented by the area score, with higher area scores indicating better discriminating ability.

3. Results

Table 1 shows the summary statistics of the 50% seen motion thresholds and the interquartile ranges of the probit fitted frequency-of-seeing curves for the controls, glaucoma suspect and glaucoma eyes.

Both the motion displacement thresholds (MDTs) and the interquartile ranges were highest in the glaucoma eyes, and lowest in the controls. Glaucoma suspect eyes were intermediate. Analysis showed a highly significant ranked difference between the groups for both variables (Kruskal–Wallis test $P<0.0001$). Post hoc two sample Mann-Whitney U tests identified significantly elevated MDTs in the glaucoma eyes ($P<0.0001$) and in the glaucoma suspect eyes ($P<0.001$), compared to controls. The interquartile ranges were also significantly elevated in the glaucoma eyes ($P<$

Table 1
Summary of the statistics for the frequency-of-seeing curves

Group	Normals (29 eyes)	Glaucoma suspects (28 eyes)	Glaucoma patients (29 eyes)
Motion threshold	5.9 ± 1.7 (2.6–8.9)	8.7 ± 3.4 (5.0–17.6)	12.9 ± 5.8 (5.2–34.2)
Interquartile range	3.3 ± 1.4 (1.0–5.9)	5.3 ± 2.3 (2.1–9.60)	8.4 ± 4.7 (4.2–25.5)

Values shown are mean ± 1 SD in min arc.
Figures in brackets indicate minimum and maximum values.

0.0001) and in the glaucoma suspect eyes ($P < 0.005$) compared to the controls. The MDTs in the glaucoma eyes were also significantly raised compared to the suspect eyes ($P = 0.0001$), as were the interquartile ranges ($P < 0.01$).

Subgroup analysis did not show any significant difference between the glaucoma suspect fellow eyes of glaucoma patients and eyes of glaucoma suspects or ocular hypertensives in terms of motion threshold, interquartile range, or Humphrey MD.

Logistic regression analysis incorporating both the motion thresholds and the interquartile ranges was performed for normal against glaucoma eyes, and for normal against suspect eyes. In both cases, the interquartile ranges (slope) and the threshold were found to contribute to the model significantly ($P > 0.05$).

To investigate the separation between the glaucoma eyes and the controls we plotted a ROC curve (Fig. 2A) of the motion threshold compared with the logistic regression model incorporating the interquartile range. A motion threshold cut-off of 9.0 min arc identified 22/29 glaucoma eyes as abnormal, with a sensitivity of 76% and a specificity of 100%. The logistic regression model incorporating both the threshold and interquartile range identified 24/29 glaucoma eyes as abnormal with a sensitivity of 83% at 100% specificity. Consideration of the interquartile range alone identified 23/29 eyes as abnormal, with a sensitivity of 79% at 100% specificity. Thus in the glaucoma eyes, only two additional eyes were identified as abnormal on the basis of an abnormal interquartile range, whereas they would have been classified as normal on the basis of threshold alone. Of the 24/29 eyes classified as abnormal by the regression model, 17/24 eyes had normal Humphrey 24-2 field thresholds at the motion test site. One such example is shown in Fig. 1D, which shows an abnormal frequency-of-seeing curve with an elevated threshold and interquartile range, indicating an abnormally shallow slope, obtained in a region of field with normal Humphrey 24-2 thresholds (Fig. 1C).

In the glaucoma suspects the motion threshold alone identified 6/28 suspect eyes as abnormal, with a sensitivity of 21% at 100% specificity (Fig. 2B). The logistic regression model incorporating the interquartile range identified 15/28 glaucoma eyes as abnormal resulting in a sensitivity of 54% with 100% specificity. The interquartile range alone identified 14/28 eyes as abnormal (sensitivity of 50% at 100% specificity). All 28 suspect eyes had normal Humphrey 24-2 fields according to our enrolment criteria. Thus amongst suspects

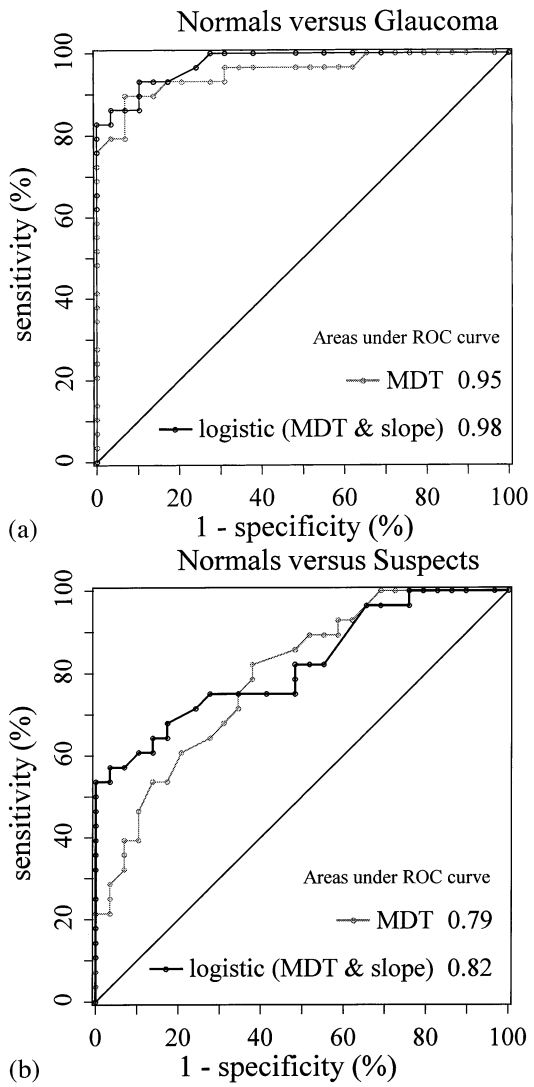

Fig. 2. Receiver operating characteristic (ROC) curves for the motion thresholds (grey line) in comparison to the logistic regression model incorporating the interquartile range (black line). (a) The ROC curve for glaucoma eyes versus controls. Areas under the ROC curve were 0.95 for the motion thresholds, and 0.98 for the logistic regression model. (b) Shows the ROC curve for suspect eyes versus controls. Areas under the ROC curve were 0.79 for the motion thresholds, and 0.82 for the logistic regression model.

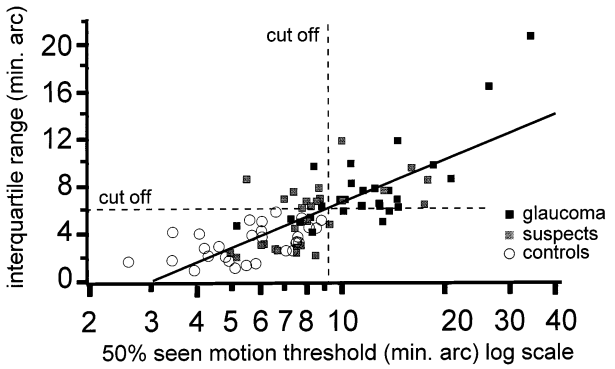

Fig. 3. Relationship between calculated interquartile range and threshold of motion frequency-of-seeing curves for all subjects. The solid line represents the least-squares linear fit through the data. Dashed lines represent cut-offs below which all of the control values for motion threshold (vertical) and interquartile range (horizontal) lie. One subject's data could not be well enough described by the probit to warrant inclusion in the graph because even at 18 min arc displacement the subject only saw the line occasionally.

abnormal ranges without abnormal thresholds were more common, accounting for nine of the 15 abnormal results. The difference between the proportion of suspects identified as abnormal using the regression model compared to the threshold alone was statistically significant (proportion test $P < 0.05$).

Thus abnormal slopes would seem to indicate early progression of the disease which may not be measurable by the threshold alone. This is shown schematically in Fig. 3 which shows the relationship between the interquartile range and the threshold. The top left hand quadrant contains the nine suspect and two glaucoma eyes which could be diagnosed as abnormal on the basis of an abnormal interquartile range when consideration of the threshold alone would class them as normals. We investigated the correlation between the threshold and the interquartile range which was significant for all subjects ($P < 0.0001$, $r^2 = 0.56$, excluding one outlier $r^2 = 0.71$). Analysis within groups showed a significant correlation between the threshold and the interquartile range at $P < 0.005$ for the controls ($r^2 = 0.27$), glaucoma suspect eyes ($r^2 = 0.32$) and for the glaucoma patients ($r^2 = 0.41$). Although statistically significant, the degree of correlation between threshold elevation and shallowing of the slope of the frequency-of-seeing curve was low, and we observed considerable variation in the slope of the frequency-of-seeing curve for a given threshold value, both within and between the subject groups. This is illustrated in Fig. 4A–C which show frequency-of-seeing curves from patients with similar motion thresholds, with markedly different interquartile ranges. Although these subjects had essentially the same thresholds (8.4–8.6 min arc) the interquartile ranges increased roughly in proportion to the seriousness of their glaucoma: extending from a normal value of $4.2 \pm$ SE 0.8 min arc for a suspect eye (Fig. 4A) to $9.6 \pm$ SE 2.2 min arc in a glaucoma eye (Fig. 4C). In contrast, we identified four eyes that had abnormal motion thresholds with normal interquartile ranges that were within the control range. Fig. 4D illustrates the frequency-of-seeing curve obtained from a glaucoma eye with an abnormal motion threshold (13.2 min arc) and a normal interquartile range ($5.1 \pm$ SE 1.0 min arc).

4. Discussion

The aim of this study was to examine the characteristics of frequency-of-seeing curves for a motion stimulus in normals, glaucoma suspects and glaucomatous eyes. We have found a correlation between the slope of the frequency-of-seeing curve and the motion threshold, with increasing threshold elevation associated with shallowing of the slope of the frequency-of-seeing curve, signifying a higher threshold variability. However the degree of association was low, and we identified considerable variation in the slope of the frequency-of-seeing curves for a given motion threshold.

A significant finding in this study was that the analysis of the interquartile range (slope) in addition to the motion threshold achieved a better separation of suspects from controls than could be obtained by analysing the motion threshold alone. A multivariate logistic regression analysis (using a forward selection procedure) was used to develop a discriminant function to separate glaucomatous eyes from controls, and suspect eyes from controls. In both cases a term using the slope data was found to contribute significantly to the model ($P < 0.05$). This supports the hypothesis that the slope provides extra information allowing for a better discrimination or separation between both suspects and controls, and glaucomatous eyes and controls.

This is reflected by the improvement in the sensitivity of the motion test in the suspects at 100% specificity from 21% using threshold alone to 54% using both variables. The improvement in separation was most marked in patients with only moderately elevated thresholds or with thresholds within the normal range. For example, only 6/28 (21%) of the glaucoma suspects had abnormally elevated motion thresholds outside our normal range. Of the remaining 22 eyes with normal thresholds, analysis of the interquartile range identified an abnormal shallowing of the slope in a further nine eyes.

In the glaucoma eyes, abnormally elevated thresholds and interquartile ranges coexisted in a high proportion (72%). Because of the greater proportion of threshold abnormalities in this group, analysis of the interquartile range only identified two additional eyes as abnormal, compared with the threshold analysis alone.

A caveat of this analysis is that whilst we have developed a discriminant function or classification rule

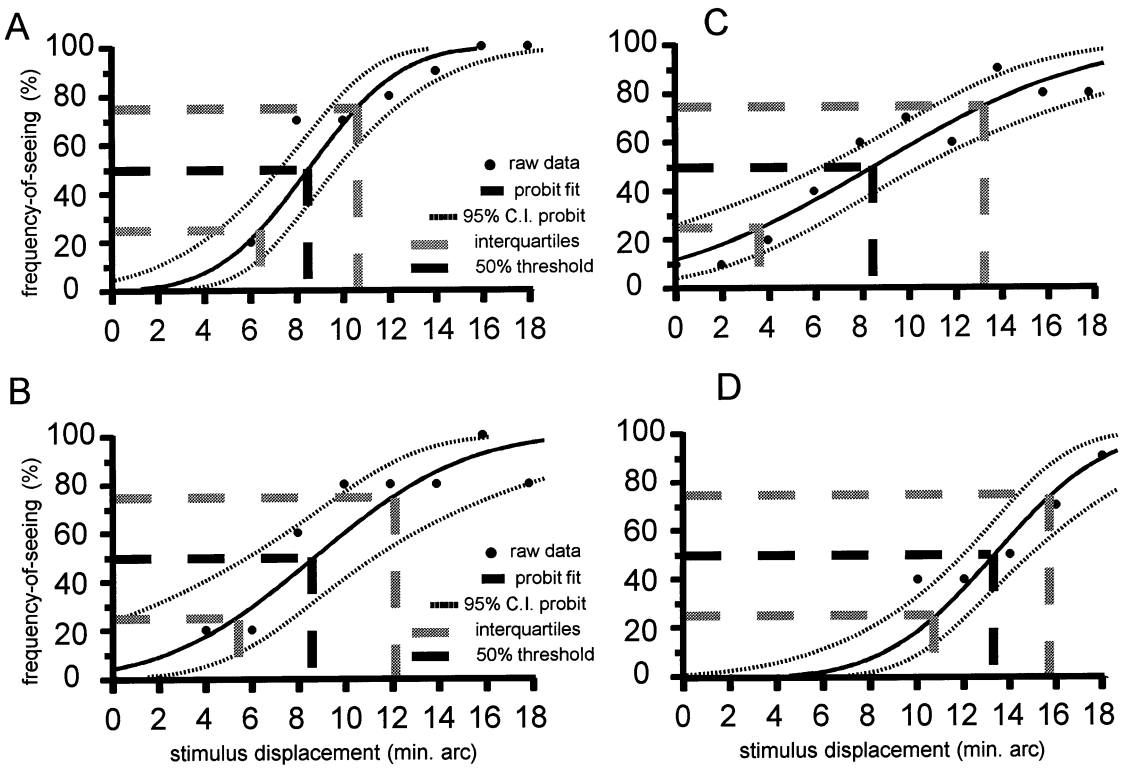

Fig. 4. Frequency-of-seeing curves from three patients with near identical normal motion thresholds (8.4–8.6 min arc), with differing slopes: (A) glaucoma suspect eye from patient aged 63 with normal interquartile range of 4.2 ± SE 0.8 min arc; (B) glaucoma suspect eye from patient aged 68 with abnormally shallow slope and elevated interquartile range of 6.8 min arc; and (C) POAG eye from patient aged 31 with marked shallowing of the slope, with elevated interquartile range of 9.6 ± SE 2.2 min arc. The threshold remains within normal limits. Frequency-of-seeing curve of POAG eye from patient aged 75 with elevated threshold (13.2 ± SE 0.7 min arc) and normal slope, indicated by interquartile range of 5.1 ± SE 1.0 min arc.

we cannot comment on its performance on an independent set of data. Moreover, the multivariate logistic regression model not only considered the threshold and the slope but also their squared terms. A different result would be obtained if we had, for example, not included the squared (quadratic) terms in the model. In fact, the squared terms were not significant ($P < 0.05$) or included for the separation of glaucomatous eyes from controls but did affect the separation of suspects from controls. The sensitivity of a discriminant function based on the threshold and slope alone (without the squared terms) in separating suspects from controls would be 43% (12 out of 28 suspect eyes identified as abnormal) at 100% specificity. Nevertheless, this is still superior to using the threshold information alone (21% sensitivity at 100% specificity) and the analysis employed does characterise the extent to which the slope provides new diagnostic information. Subsequent studies may validate it as a usable method.

Our findings of a correlation between the motion threshold and slope of the frequency-of-seeing curve is analogous to that for conventional perimetry, which has been reported by a number of researchers (Chauhan & House, 1991; Weber & Rau, 1992; Olsson, Heijl, Bengtsson & Rootzen, 1993; Chauhan, Tompkins, LeBlanc & McCormick, 1993; Henson, Evans, Chauhan & Lane, 1996; Wall, Maw, Stanek & Chauhan, 1996). The considerable individual differences that we identified in the motion frequency-of-seeing curves of patients with similar motion thresholds are similar to the findings of Chauhan, Tompkins, LeBlanc & McCormick (1993) for a luminance stimulus.

Our results indicate that an abnormal shallowing of the slope of the motion frequency-of-seeing curve may represent one of the earliest changes in glaucoma, and may occur before identifiable threshold elevation. This finding suggests that measures of intratest variability may be an important component of future motion tests in glaucoma. Further longitudinal studies are required to investigate whether frequency-of-seeing analysis can improve the sensitivity and specificity of motion testing in predicting conventional field deterioration.

In addition to the use of frequency-of-seeing analysis, a further improvement in our line displacement test may be achieved with the use of lower contrast stimuli. Lee, Wehrhahn, Westheimer & Kremers (1993) have shown that individual parvocellular cells (at 8° retinal

eccentricity) were capable of responding to line displacements of as little as 2 min arc as long as the contrast was 40% or greater. They reported parvocellular mediated displacement thresholds of 4 min arc. This is similar to the smallest sized thresholds we obtained in normals in the present study using a line stimulus of the same width (2 min arc). In future it may be advantageous to use a lower contrast line stimulus for our MDT test in order to better isolate magnocellular responses.

The cause of the increased variability that we have observed in the motion testing of our patients with glaucoma remains unknown. A number of mechanisms have been proposed to explain the increased variability reported in glaucoma for conventional field testing, and similar mechanisms may be invoked to explain our findings for motion testing.

One hypothesis is that small inaccuracies of fixation in the presence of steep field threshold sensitivity profiles may account for the increased variability in glaucoma (Henson & Bryson, 1990/1991; Haefliger & Flammer, 1991; Vingrys & Demirel, 1993). According to this hypothesis, the degree of variability would be expected to depend on the magnitude of fixation instability and the number and steepness of the sensitivity gradients. However Henson, Evans, Chauhan & Lane (1996) have recently cast doubt on this hypothesis by measuring perimetric frequency-of-seeing curves both with and without fixation error correction in 14 glaucoma patients. They identified a positive correlation between the sensitivity and the slope of the frequency of seeing curve, with a shallowing of the curve associated with locations of lowered sensitivity. A reanalysis using only those responses with good fixation had no significant effect on reducing the variability, either at normal locations or damaged field locations (Henson, Evans, Chauhan & Lane, 1996).

Alternative mechanisms which are not dependent on fixation losses have been proposed to explain the changes in the slope of the psychophysical function. These include neural mechanisms related to factors such as fatigue (Brenton & Argus, 1987) and reduced number of nerve fibres (Flammer, Drance & Zulauf, 1984). We have considered our findings in terms of the concept of reduced redundancy, as proposed by Johnson (1994).

One prediction of the reduced redundancy hypothesis is that selective tests should exhibit greater threshold variability than non selective tests. This is because a selective test stimulates a sparser subpopulation of ganglion cells with minimal overlapping receptive fields, compared with more non-selective tests (Johnson, 1994). This prediction of the reduced redundancy hypothesis has been supported by Wild, Moss, Whitaker & O'Neill (1995), who have shown that the short term variability of selective blue-on-yellow testing (SWAP) is higher than conventional perimetry (Wild, Moss, Whitaker & O'Neill, 1995). This mechanism may underlie our finding that a high proportion of patients have significant shallowing of the slope of the motion frequency-of-seeing curve, signifying high intratest variability.

Our findings suggest that the analysis of intratest variability in motion testing can identify important additional differences between glaucoma patients and controls. This may lead to improvements in our understanding of the earliest abnormalities of motion sensitivity in glaucoma.

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